COFFIN et al.
Appl. No. 09/762,098
December 1, 2003

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REMARKS

Reconsideration is requested.

The specification has been amended to include a cross-reference to the parent application. The applicants submit that the time periods for making such an Amendment, as described in Rule 78(a)(5)(ii) do not apply, pursuant to the exception provided in Rule 78(a)(5)(ii)(B). The Examiner is requested to advise the undersigned however if anything further is required in this regard.

The Patent Office has acknowledged receipt of the priority document from the International Bureau. See, Notification of Acceptance dated June 28, 2001. The Examiner is requested to confirm the same by indication on page 1 of the next Office Action or Notice of Allowance.

The Section 102 rejection of claims 1, 5 and 7 over Moriuchi *et al.* (J. Virol., 1993, Vol. 67, pp. 2739-2746) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing remarks.

Independent Claim 1 is directed to a process for preparing a pharmaceutical composition comprising the step of formulating the mutant HSV with a pharmaceutically acceptable carrier or diluent. The applicants submit that Moriuchi *et al.* teaches that the yield of HSV-1 *in*1814 may be increased by growing the virus on cells expressing VZV ORF10. Moriuchi *et al.* does not however teach that HSV-1 *in*1814 may then be harvested and purified. Accordingly, Moriuchi *et al.* does not disclose HSV-1 *in*1814 produced using a VZV ORF cell line contained in a pharmaceutically acceptable carrier or diluent. The Examiner's reliance on an alleged inherent teaching of the cited art at

page 3 of the Office Action dated July 29, 2003 (Paper No. 19) is not supported by any evidence of record.

Moreover, the paragraph referred to by the Examiner (page 2744 line 9 first column to line 6 second column) does not relate in any way to the *in*1814 mutant HSV-1 grown on VZV ORF10 expressing cells. This paragraph is understood by the applicants to describe the production of infective wild-type HSV-1 virus following the introduction of wild-type HSV-1 DNA into cells (see page 2743 last two lines to page 2744 lines 1 to 8).

The experiment described at page 2744 shows that production of infective wild-type HSV-1 virus following the introduction of wild type HSV-1 DNA into cells expressing VZV ORF is enhanced compared to production following transfection of control cells. The HSV-1 DNA used in these experiments does not comprise a mutation in the VP16 gene. Accordingly, the virus produced by the VZV ORF10 expressing cells is wild-type HSV-1 that expresses a wild-type VP16 gene. It is this wild-type virus that was harvested and cultured as described in Moriuchi *et al.* at page 2744. Moriuchi *et al.* does not disclose a method comprising the steps of propagating a herpes simplex virus having a mutation in its endogenous VP16 gene using a VZV ORF expressing cell line, isolating the herpes simplex virus and formulating the isolated herpes simplex virus in a pharmaceutically acceptable carrier or diluent. The cited reference therefore fails to teach, literally or inherently, each and every aspect of the presently claimed invention.

Claims 1, 5 and 7 are submitted to be patentable over Moriuchi and withdrawal of the Section 102 rejection over the same is requested.

The Section 103 rejection of claims 1, 3-5, 7-10, 27 and 28-58 over Speck *et al* (WO96/04395 A1)., Moriuchi *et al.* and Purewall *et al.* (Virology 1994, vol 198, pp. 385-

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389) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing remarks.

Speck *et al.* teaches that the VP16 mutation in the HSV should be one that allows growth in the presence of hexamethylene bisacetamide (HMBA) (page 4 lines 3 to 6) and teaches that the mutant virus should be grown in the presence of HMBA (page 27 lines 25 to 35). Speck *et al.* also addresses the issue of growing mutant viruses on a complementing cell line (see page 6 line 21 to page 7 line 14) giving IE0, IE4, IE27 and gH as examples of mutated genes that may be complemented in a cell line. However, the applicants submit that Speck *et al.* does not teach or suggest that a mutation in the VP16 gene may be complemented using a cell line. In fact, Speck *et al.* is believed to teach away from using a cell line to complement the mutated VP16 gene stating that "*it is preferred, however, not to complement a mutation in the VP16 gene in the complementing cell line, since the effect of the mutation in this particular gene is considered to be obtained where the mutant gene product forms part of the virion*" (see page 7 lines 8 to 12). Hence, one of ordinary skill in the art reading Speck *et al.* may have appreciated that, in theory, VP16 expressed in a cell line could have been used to complement a mutation in the VP16 gene of the HSV but that such complementation would not have been desirable where the mutant virus was intended for use as a pharmaceutical vaccine or vector.

Moriuchi *et al.* teaches that VZV ORF10 could have been used to increase the yield of the HSV-1 *in*1814 mutant. One of ordinary skill in the art may, therefore, have appreciated that VZV ORF10 can complement an HSV VP16 mutation. However, Moriuchi *et al.* is not at all concerned with the production of safe mutant herpes viruses

suitable for use as pharmaceutical vectors or vaccines. Accordingly, Moriuchi *et al.* provided no teaching or suggestion to one of ordinary skill in the art as to whether expression of the VZV ORF10 gene in a complementing cell line may or may not have been a suitable alternative to HMBA in the propagation of HSV vectors or vaccines comprising a mutation in the VP16 gene.

Similarly, although Purewall *et al.* teaches that EHV-1 and EHV-4 homologs of VP16 strongly transactivate HSV-1 IE genes, this document is not concerned with the production of safe mutant herpes viruses for use as vaccines or vectors. Accordingly, Purewall *et al.* did not provide the skilled person with any guidance as to whether or not a VP16 mutant HSV for use as a pharmaceutical could have been grown in the absence of HMBA on a complementing cell expressing a EHV-1 or EHV-4 homolog of VP16.

Thus, neither Moriuchi *et al.* or Purewall *et al.* taught or suggested that use of a VP16 homolog in a complementing cell line is a safe alternative to using HMBA to promote growth of a VP16 mutant HSV. Neither document would have led a person of ordinary skill in the art away from the teaching in Speck *et al.* that a mutation in the VP16 gene of HSV should not be complemented in a cell line used for the production of vectors or vaccines for pharmaceutical use, but compensated for using HMBA. A person of ordinary skill in the art at the time that the invention was made would not, therefore, have been motivated to propagate a VP16 mutated HSV for use in a pharmaceutical formulation using a complementing cell line expressing a VP16 homolog. Accordingly, the presently claimed invention would not have been obvious over Speck *et al.* in view of Moriuchi *et al.* and Purewall *et al.* Withdrawal of the Section 103 rejection is requested.

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Having fully responded to all of the pending rejections and objections contained in Paper No. 19, Applicants submit that the claims are in condition for allowance and earnestly solicit an early notice to that effect.

Respectfully submitted,

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C#/M#: 117-340
Serial No.: 09/762,098 Atty: B. J. Sadoff
Inventor/s: COFFIN et al. Date: Dec. 1, 03
Title: CELL LINES FOR THE PROPAGATION OF MUTATED HERPES VIRUSES

XX Amendment Under Rule 116

$ Fee (Check) - **Pre-Bill**
$55.00 Fee (Check) - Non Pre-Bill

$55.00 Total Fee Enclosed

Other: **Extension Petition and Fee (One Month Extension - Small Entity)**

PATENT APPLICATION INFORMATION RETRIEVAL

Search results for application number:09/762,098			
Application Number:	09/762,098	Customer Number:	23117
Filing or 371(c) Date:	06-20-2001	Status:	Final Rejection Mailed
Application Type:	Utility	Status Date:	07-28-2003
Examiner Name:	LI, BAO Q	Location:	ELECTRONIC
Group Art Unit:	1648	Location Date:	12-17-2003
Confirmation Number:	7947	Earliest Publication No:	-
Attorney Docket Number:	117-340	Earliest Publication Date:	-
Class/ Sub-Class:	424/229.1	Patent Number:	-
First Named Inventor:	Robert Stuart Coffin, London, (GB)	Issue Date of Patent:	-
Title Of Invention:	Cell lines for the propagation of mutated herpes viruses		

File Contents History

Number	Date	Contents Description
35	07-29-2003	Mail Final Rejection (PTOL - 326)
34	07-28-2003	Final Rejection
33	07-18-2003	Petition Decision - Dismissed
32	08-16-2002	Petition Entered
31	05-06-2003	Information Disclosure Statement (IDS) Filed
30	05-09-2003	Date Forwarded to Examiner
29	05-06-2003	Response after Non-Final Action
28	05-06-2003	Request for Extension of Time - Granted

27	12-30-2002	Correspondence Address Change
26	11-06-2002	Mail Non-Final Rejection
25	11-04-2002	Non-Final Rejection
24	08-16-2002	Miscellaneous Incoming Letter
23	08-22-2002	Date Forwarded to Examiner
22	08-16-2002	Response to Election / Restriction Filed
21	08-16-2002	Request for Extension of Time - Granted
20	08-16-2001	Information Disclosure Statement (IDS) Filed
19	05-16-2002	Mail Restriction Requirement
18	05-15-2002	Requirement for Restriction / Election
17	03-14-2002	Case Docketed to Examiner in GAU
16	08-15-2001	Case Docketed to Examiner in GAU
15	06-20-2001	Preliminary Amendment
14	06-20-2001	Information Disclosure Statement (IDS) Filed
13	06-20-2001	Affidavit(s) (Rule 131 or 132) or Exhibit(s) Received
12	07-18-2001	Application Dispatched from OIPE
11	07-13-2001	IFW Scan & PACR Auto Security Review
10	07-02-2001	Correspondence Address Change
9	06-28-2001	Released to OIPE
8	06-28-2001	Notice of DO/EO Acceptance Mailed
7	06-20-2001	Applicant 371 Filing Paper Received
6	02-26-2001	Notice of DO/EO Missing Requirements Mailed
5	02-24-2001	371 Application Preexamination Docketing
4	02-14-2001	371 Application Preexamination Docketing
3	02-02-2001	Receipt of 371 Request
2	02-14-2001	Correspondence Address Change
1	06-20-2001	Initial Exam Team nn